REMARKS

Claims 1- 27 are under examination and have been rejected. Claim 1 has been amended.

Rejection Based on 35 U.S.C. 102(b)

Claims 1-14 and 20-27 were rejected under 35 U.S.C. 102(b) as being anticipated by Kihara et al (Cancer Res. 61: 6474 (2001)), which discloses analysis of gene expression profiles (such as at Figure 2) for various anti-cancer drugs in 20 patients (noted in the Abstract). The Examiner also contends that Kihara teaches "classification of esophageal tumor cells based on gene expression data, determination of therapy, and prediction of patient outcome" (Office Action at page 2, lines 10-12).

Applicants respectfully traverse this ground of rejection. Claim 1 has been amended to better reflect the claimed invention. Amendment of claim 1 adds no new matter and is fully supported in the claims and specification as filed. Claim 1, prior to amendment, recited the steps of identifying in a test (or different) cell the expression profile of a gene set present in a susceptible cell but without contacting with a drug and where the susceptibility depended on a change in the expression profile of the susceptible cell. Thus, the change in profile would have had to be measured to determine the affected gene set and amended claim 1 recites this difference as being either measured or already known.

Further, the application (at page 10, lines 11-21, describes a set of genes whose expression profile is altered by contact with a test compound wherein said change determines susceptibility and absence of contacting determines the basal expression profile so that the same gene set in a different cell not contacted with the drug is also deemed an affected set. Amended claim 1 more clearly makes this comparison. In

addition, a susceptible cell includes cells that respond to drug treatment with gene movements (see application at page 10, lines 28-30). As the application teaches, other cells (different or test cells) are determined by finding the same basal expression pattern in those cells as for the untreated susceptible cell (at page 15, lines 7-16, and page 16, lines 22-24, where use of a database (i.e., one source of existing information) is taught) .

To anticipate a claim, the prior art reference must disclose each limitation of the claim. For example, Applicants' amended claim 1 comprises the steps of first determining a gene expression profile and then comparing it to the profile of the same gene set of a drug-susceptible cell without drug treatment but where the profile of said susceptible cell is known to be affected by drug treatment, i.e., there is a change in profile after drug treatment.

Conversely, Kihara et al. (2001) simply analyzes a gene expression profile in a tumor removed from a patient prior to treatment of the patient with an anti-cancer drug (for example, 5-fluorouracil). Said drug is then administered to the patient as a means of killing residual cancer cells not removed by the surgery. Kihara does not appear to disclose any gene expression profile in cells of the cancerous tissue after contacting these cells with said drug. Thus, Kihara's concept does not involve determining a cell susceptible to treatment with a test compound by comparing a gene expression profile of a gene set for such cell to a gene profile of such set of genes of a cell where such set of genes has been determined to have a change in gene expression profile with and without treatment with the test compound and where such cell is susceptible to treatment with the test compound. Kihara does not show that he has the right gene set because he never contacts the cells with the drug to see if the selected genes alter expression after said contact.

Applicants' claim 12 is similar to claim 1 but recites determining inhibition of growth of the susceptible cell in addition to the basal expression profile so that again

Kihara does not anticipate all of the elements of Applicants' claims. In addition, because Applicants' treatment claims are drawn to use of the agent from such screens not taught by Kihara, the latter reference is inapposite to anticipate the treatment claims as well. Applicants' claim 20 is drawn to treatment and not prognosis, in particular, treatment of a disease caused by the different, or test, cell determined by the methods of the claims.

Claims 1-12, 15-19, and 23-25 were rejected under 35 U.S.C. 102(b) as being anticipated by Scherf et al (Nature Genetics 24: 236 (2000)), which the Examiner contends teaches analysis of gene expression profiles by using a protein expression database...in connection with cancer cells' response to anti-cancer drugs." (see Office Action at page 2, lines 14-16)

Applicants' claims (including amended claim 1) have been described above and Applicants contend that they are not anticipated by Scherf et al. (2000) for reasons similar to Kihara et al. In contrast, Scherf looks at a single cell line versus many drugs and then looks for clustering. Unlike Applicants' claimed methods, Scherf does not look for other cells that might be susceptible but, instead, does what amounts to a standard gene profile against different drugs present in a database using 60 different cell lines. Scherf does not use his results to identify any additional susceptible cells or cell lines and thus does not teach Applicants' claimed method, i.e., finding a different cell that is also susceptible by comparing the gene profile of the different cell with the profile in the susceptible cell when neither is contacted with the test compound.

Scherf first organizes the cell lines based on gene expression patterns without looking for susceptible cells (see page 237, column 1, second full paragraph), then looks at drug activity profiles to cluster the 60 cell lines based on growth inhibitory activity (page 237, column 2, second full paragraph under "Cell-cell correlations") to find sensitive cell lines and finally compares the two patterns (page 238, column 2, paragraph under "Gene-drug correlations") to conclude that they are not the same. In

other words, Scherf compares the expression profile of a gene set across 60 cell lines with the growth inhibitory activity of 118 drugs across those same 60 cell lines. However, Scherf does not determine any expression profile in the cells after drug treatment and so therefore never determines that drug susceptibility is due to change in expression profile as recited in Applicants' claim 12 (step(b)) or amended claim 1. Scherf even states that his "gene expression patterns were determined in untreated cells" (at page 241, column 2, lines 2-4 under "Discussion") and that "we generated our activity database using only...short term growth inhibition and cytotoxicity" (at page 242, column 1, lines 6-8). Because Scherf does not teach all of the steps of Applicants' claims his teaching does not anticipate them.

Neither Scherf nor Kihara identify cells susceptible to treatment by use of a gene set that has a change in gene expression profile as a result of use of a test compound in a cell susceptible to treatment with such test compound by comparing gene profiles in absence of said treatment in order to determine other cells susceptible to treatment with such test compound. As a result, such references do not anticipate the claims.

Applicants believe that the grounds of rejection have been overcome and that the claims are in condition for allowance.

Request for 3 month extension of time and required fee are enclosed. No additional fees are believed due in filing this response. The Commissioner is authorized to charge payment of any additional fees required under 37 CFR 1.16 associated with this communication or credit any overpayment to Deposit Account No. 03-0678.

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Respectfully submitted,

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